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EXAMINER

TURNER, SHARON L

ART UNIT PAPER NUMBER

1649

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/316,387	Applicant(s) SOLOMON ET AL.	
	Examiner Sharon L. Turner	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3-13-06.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24, 28 and 30-49 is/are pending in the application.
 4a) Of the above claim(s) 28 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24, 30-35 and 37-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 24, 28 and 30-49 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Response to Amendment

1. The Examiner and/or Art Unit of U.S. Patent application SN 09/316,387 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1649.
2. The amendment filed 12-20-05 has been entered into the record and has been fully considered. Claims 24, 28 and 30-49 are pending.
3. The Declaration filed 12-20-05 under 37 CFR 1.131 via Alan Solomon, Rudi Hrcic and Jonathan Stuart Wall has been entered into the record. However, the declaration is unexecuted and further the Exhibits referred to therein have not been provided. Accordingly, the declaration is ineffective to overcome any ground of rejection and it has not been considered further.
4. In a telephone inquiry on 3-29-06 Applicant's representative Edward Amaya notified the Examiner that a signed copy of the aforementioned declaration was transmitted to the office on 3-6-06. This signed copy was not available to the Examiner during the preparation of the 3-13-06 Office Action as it crossed in the mail. This Office Action replaces the action of 3-13-06, considers the signed declaration and resets the time period for response.
5. The 3-13-06 declaration via Solomon, Hrcic and Wall is not persuasive to remove the '427 and '523 patents from instant claims. The declaration is on point to antibodies anti- κ 1 (57-18H12) (mouse monoclonal to κ 1 light chain amyloid) and anti- κ 8 (31-8c7) (mouse monoclonal to κ 8 light chain amyloid). The antibodies are shown to

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bind to different light chain amyloids and to Abeta 25-35 as noted in exhibit A and point 5, and to be effective for removal of *unspecified* "amyloidoma masses" as noted in exhibit B and point 6. However, this evidence is not fully commensurate in scope with the claims. Claim 24, is generically directed to "opsonization of an amyloid fibril and induces removal of amyloid deposits." Similarly, claim 46 is specifically directed to "opsoniz(ation of) a non-light chain amyloid fibril and induces removal of amyloid deposits." Binding in vitro, as in exhibit A, is not demonstrated or evidenced to be predictive of opsonization or removal in vivo. As noted previously, exhibit B is silent as to the form of amyloid being opsonized and the specification is only on point to opsonization and removal of light-chain amyloid, not to other amyloid fibrils such as, but not limited to, beta amyloid. Accordingly the declaration is not supportive of the scope of the claims directed to removal of amyloids other than light chain amyloid and specifically to non-light chain amyloid as recited in claims 46-49. It is further noted that the antibodies exemplified are mouse monoclonals, and not representative of human, humanized or chimeric antibodies. Accordingly, the scope of the claims is outside the scope of the declaration and the declaration therefore is not persuasive to remove the noted reference with respect to those claimed teachings. However, amendment to opsonization or removal of light chain amyloid would appear to be in scope with the evidence demonstrated with antibodies anti-κ1 (57-18H12) (mouse monoclonal to κ1 light chain amyloid) and anti-κ8 (31-8c7) (mouse monoclonal to κ8 light chain amyloid).

6. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

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7. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn.

Election/Restriction

8. Applicant's election with traverse of species monoclonal antibodies reactive with a non-light chain amyloid, identified by applicants as claims 23-36 and 39-45 in Paper No. 14 (2-4-02) is acknowledged. The traversal is on the ground(s) that the Office Action fails to provide evidence of any significant search burden with respect to the delineated species. This is not found persuasive because as set forth the species are patentably distinct as they lack a common core structure and differ in functional properties with different use, different modes of operation, different functions and different effects. Thus a search for any one of the species would not reveal all pertinent art to any other species and thus the search and examination of all species in a single application may place an undue burden upon the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

9. As set forth in Paper No. 15, mailed 4-23-02, newly submitted claims 28 and 36 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicants have elected species of monoclonal antibodies reactive with a non-light chain amyloid. Applicants have identified the elected invention as readable on claims 28 and 36. However, claims 28 and 36 are drawn to antibodies raised against immunoglobulin light chain and to monoclonal antibodies reactive with immunoglobulin light chains and thus are directed to non-elected species.

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Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28 and 36 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

In the response of 12-20-05 Applicants request consideration of withdrawn claims 28 and 36 on the basis that antibodies raised against immunoglobulin light chain react with non-light chain amyloid, such as AA-amyloid ("AA" is an uncertain abbreviation here) fibrils made from A β protein (non-light chain amyloids) as supported at p. 20, lines 7-14 and further that the monoclonals deposited may recognize an epitope that is a general feature of amyloids as at p. 18, lines 17-21 and Example 6.

This argument has been fully considered but is not persuasive. The scenario derived by Applicants above is in opposite to the election noted. The search was directed to antibodies or immunoglobulin polypeptides that opsonize/react with a non-light chain amyloid. Such genus is inclusive of beta amyloid as noted in the claims. However, the fact that a specific antibody generated with specificity to light chain amyloid cross-reacts with beta-amyloid does not evidence that the opposite is true, ie., that an antibody generated with specificity to beta-amyloid will necessarily react with light chain. Antibodies are commonly identified with respect to the antigens to which they were generated. Here, it is of common knowledge in the art that the antigens/proteins differ. Light chain amyloids are a different class of proteins than non-light chain proteins and the amino acid sequences do not share homology or similarity

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in sequence. In other words, the genus is non-coextensive and is mutually exclusive, ie., the species and/or subgenus are not of the same scope. A search for antibodies that opsonize and/or react with non-light chain amyloid is not the same as, nor co-extensive with a search for such antibodies generated to light chain amyloids. Accordingly restriction is proper and withdrawal of the non-elected invention is maintained.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 24, 30-35, and 37-49 rejected under 35 U.S.C. 102(e) as being anticipated by Schenk US Patent No., 6,743,427, June 1, 2004.

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12. Claims 24, 30-35, and 37-49 rejected under 35 U.S.C. 102(e) as being anticipated by Schenk US Patent No., 6,787,523, September 7, 2004.

The aforementioned US Patents are cumulative, see in particular the '427 patent is a continuation in part of the '523 patent. Thus, the rejections are noted together. The claims of the 6,743,427 are most relevant in that the claims are directed to a method of prophylactically or therapeutically treating Alzheimer's disease comprising administering to the patient an effective dosage of a pharmaceutical compositions comprising an antibody that specifically binds to an epitope within residues 1-12 of Abeta wherein the isotype of the antibody is human IgG1, see in particular claims 1-19. However, the details of the rejection will be set forth with citation to the '523 patent, reflecting the disclosure most similar to the effective filing date of 12-2-1997.

The '427 and '523 patents each teach treatment of Alzheimer's disease via either administration of peptide to promote the production of beta amyloid antibodies (Active immunization) within the host or via direct administration of antibodies (Passive immunization) reactive to beta amyloid, see in particular columns 1-4, 10-11, column 14, lines 55-63, and columns 33-34 Passive immunization. The Patent teaches that the mechanism whereby the active immunization treatment is effective is via the stimulation in vivo of an antibody response with high titer sufficient whereby the antibodies bind to and remove the amyloid plaques from brain, see in particular columns 13-33. Hence the mechanism disclosed in the patent is the same as that claimed, ie., "whereby the antibody or immunoglobulin polypeptide or fragment thereof (is) in an amount effective to remove amyloid deposits, wherein the antibody or immunoglobulin polypeptide or

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fragment thereof (binds to and) opsonizes an amyloid fibril and induces removal of amyloid deposits". As in claims 30-32 and 47-49, the antibodies may be monoclonal, see in particular column 10, line 64, human, column 11, lines 15-17, humanized, column 11, lines 9-14 in particular but also column 11, lines 1-55. In particular, such humanized antibodies or portions where immunoglobulin specific chains or genes are alternatively linked constitute antibodies that are "chimeric" or "having cross-isotype reactivity" thereby anticipating claims 33-34 and 39. The antibodies may be labeled as in for detection in vitro or in vivo, see in particular Figures 5-14. The antibodies may constitute fragment portions such as Fv, Fab etc, see in particular column 11, lines 40-44, and single chain, column 11, line 43, corresponding to claims 37-38. As previously detailed the antibodies are specific to beta amyloid protein of Alzheimer's disease, corresponding to non-light chain amyloid, see also column 9. The treatment is noted to be inclusive of humans and human patients, see in particular column 8. Claim 43 presents the limitation, "wherein the antibody or immunoglobulin polypeptide or fragment thereof is reactive with an amyloid fibril other than the amyloid fibril or component or precursor thereof against which the immunoglobulin polypeptide or fragment thereof was raised." This is deemed to be an inherent property of the noted antibodies which are made either in vitro or in vivo and then isolated and or proliferate in vivo such that the progeny or administered antibodies react with amyloid fibrils in vitro or in vivo but those fibrils are other than the ones against which the antibodies were raised, a process mediated via B-cell production. As in columns 8 and 13-17 the

treatment is via administration of multiple molecules (concentration dependent) and with carrier (claims 44-45). Thus, the reference teachings anticipate the claimed invention.

Applicants argue in the 12-20-05 and 3-6-06 responses that the 1.131 declaration and exhibits obviate rejection.

Applicant's arguments filed 12-20-05 and 3-6-06 have been fully considered but they are not persuasive as noted above. The declaration and evidence referred to therein is not in scope with the claimed invention.

13. Claims 24, 30-31, 35, 39-46, 48-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Konig et al., WO96/25435, 22 August 1996

Konig et al., teach methods of diagnosis, screening and therapeutics for treating unique forms of amyloid peptide deposition including Alzheimer's disease using antibody administration, see in particular p. 6 lines 1-9, 21-22, p. 7, lines 21-27, p. 14, lines 9-11, and p. 25, lines 14-17. The embodiments include all immunological and related methodologies applied to the detection, monitoring, extraction, inhibition and modification of beta-amyloid species in the diagnosis and treatment of Alzheimer's disease, see in particular p. 25, lines 14-17. Konig et al., teach administration of monoclonal antibodies that bind amyloid fibrils, see in particular claims 9-20 and pp. 6-8, including for treatment of Alzheimer's disease. The antibodies specifically bind amyloid fibrils, see in particular p. 6, line 25. Thus, the reference teaches a method which comprises administration of beta amyloid antibodies (immunoglobulin polypeptides) for extraction (removal) of amyloid beta peptides and the treatment of Alzheimer's disease. Claims 15-16 further teach methods of preventing aggregation of

beta amyloid peptide comprising administering monoclonal antibody reactive with beta amyloid peptides as in claims 1 and 5. While the reference does not explicitly teach administration "in a patient" as recited in the claim, the artisan well recognizes that such is clearly implied by the teachings directed to therapeutic treatments of Alzheimer's disease comprising administration of the noted antibodies. In particular, Alzheimer's disease is known to be an etiology that affects human patients, particularly the elderly via amyloid plaque deposition and accumulation within the brain, see in particular Background, pp. 1-5. Konig further teaches that the antibody treatment is effective in a method for the prevention of aggregation of beta amyloid peptide by administration of the antibody, see in particular p. 7, lines 21-23, p. 13, lines 17-20, p.14, lines 6-11 and p. 25, lines 14-18, including in the extraction of beta amyloid species. As the antibodies bind beta amyloid as taught by Konig and are effective in therapeutic treatments of Alzheimer's, they are inherently effective to anticipate the claims. The antibodies can be provided in sterile saline or a pharmaceutically acceptable carrier such as Keyhole Limpet Hemocyanin, see in particular p. 17. The antibodies include human and may be labeled by biotinylation or with radioactive tags such as ³⁵S-Met, see in particular p.22-24. Konig further notes at p. 5-7 suitable cross-isotype and cross reactive antibodies and epitopes via various modifications in peptide immunogen and whether the antibody is for example monoclonal or polyclonal. Specific embodiments of monoclonals are disclosed from p. 19-23.

Applicant's argue in the response of 6-27-03 that Konig merely teaches methods of generating antibodies and methods of using the antibodies to detect amyloid in post-

mortem tissue and only shows the results of immunohistochemical studies. Applicant's argue that Konig does not teach administration of the antibodies to a patient for any reason, let alone to remove amyloid deposits. Applicant's argue that Konig does not show that their antibodies are able to remove amyloid deposits from a patient.

Applicant's additionally argue in the Biere declaration that the usefulness of antibodies as diagnostics and in binding and detecting amyloid plaques does not suggest that the antibodies are effective in removing amyloid plaques from a patient and that the reference therefore does not anticipate the claimed invention.

Applicant's arguments filed 6-27-03 have been fully considered but are not persuasive. First, Konig does teach methods of generating antibodies and methods of using the antibodies to detect amyloid in post-mortem tissue using immunohistochemical studies. Yet, Konig et al also teach the use of the antibodies in methods of treatment for Alzheimer's disease including for extraction of beta amyloid species and in therapeutic compositions for the treatment of Alzheimer's disease. In contrast to Applicant's interpretation, Konig teaches the administration of the antibodies to Alzheimer's patients which are known to be human patient subjects. It is true that Konig does not teach the definitive mechanism for the treatment provided to Alzheimer's patients via administration of antibodies to beta-amyloid. However, the mechanism of the treatment is not required for Konig to be enabling. Moreover, Konig does allude to the mechanism in part by their reference to extraction of beta amyloid species. It is well accepted in patent law that a newly discovered property does not make a compound or method newly patentable. Similarly here, the claiming of an old method via the use of

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mechanistic limitations such as the recitation of "an amount effective to remove amyloid deposits" does not evidence patentability over the prior art teachings. The question is whether or not the methods are the same or different. In this analysis both methods provide the same antibodies to the same patients for the same purpose. Moreover, Konig notes that their method is effective for treatment and thus the mechanism is inherently provided absent convincing factual evidence to the contrary. It is Applicant's burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicant's claims. Reasons showing inherency have clearly been shown and there are no limitations to the antibodies, their amounts or routes of administration that would teach over the prior art reference. Thus, the reference teachings anticipate the claimed invention.

Applicants arguments presented in the 3-3-04 response are essentially the same as in the 6-27-03 response as noted above. In essence, Applicants maintain that the Konig reference is a general description of diagnostic and therapeutic uses of amyloid antibodies and that Konig does not specifically teach removal of amyloid fibrils from a patient as is claimed.

Applicants additionally argue in the 3-30-04 response that the Konig reference is nonenabling in that it does not show that their monoclonal antibodies are effective for removal as required. Applicants cite *Minnesota Manufacturing and Mining v. Chemque Inc.*, *Elan Pharmaceuticals v. Mayo Foundation*, and *In re Wands* in support of their arguments. In particular applicants assert that Konig does not teach sufficient direction or guidance or the presence of working examples. Additionally Applicants point to the

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declaration of Dr. Biere stating that the mere binding of an antibody to an amyloid fibril for diagnostic purposes is not sufficiently predictive of its ability to remove amyloid from a patient. Applicants additionally note that the claim 49 recites that the immunoglobulin polypeptide is a monoclonal antibody raised against an amyloid fibril and accordingly Konig does not disclose all elements of this claim.

Applicants arguments presented 3-30-04 have again been fully considered but are not found to be persuasive for the same reasons of record. The question of anticipation here is whether or not the methods are the same or different. In this analysis both methods provide the same antibodies to the same patients for the same purpose. Konig teaches that the administration is for binding amyloid fibrils and for extraction of beta-amyloid species. Konig further notes that their administration is effective for treatment of Alzheimer's. Thus, while Konig does not teach *ipsis verbis* "a method of removing amyloid deposits", these claim limitations are deemed to be inherently provided as the administration is the same, i.e., an amount of immunoglobulin polypeptide in an amount effective to remove amyloid deposits wherein the immunoglobulin polypeptide or fragment thereof binds to an amyloid fibril or component or precursor thereof. A prior art reference is not required to teach the mechanism of action in order meet the requirements of either anticipation or enablement. The preamble statement "removing amyloid deposits" is akin to the recitation of a mechanism. In particular, it is Applicant's burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicant's claims. Reasons showing inherency have clearly been shown and

there are no limitations to the immunoglobulin polypeptides (antibodies), their amounts or administration that teach over the prior art reference. There is no precedent in the cited case law to conclude that Konig is non-enabled. The above appears more to a question of fact to which Applicants have shown no evidence or scientific reasoning that would disprove the Konig teachings. Applicants question of Konig's enablement alludes to a question of enablement regarding the instant claims as the Konig teachings are not differentiated therefrom. The Biere declaration as set forth below is not effective to obviate the rejection in that it does not substantiate a conclusion that the prior art of record is non-enabled. With respect to the noted limitations at claim 49, Applicants are redirected to the grounds of rejection as previously set forth. In particular, Konig et al., teach administration of monoclonal antibodies which bind amyloid fibrils, see in particular claims 9-20 and pp. 6-8, including for treatment of Alzheimer's disease. The antibodies specifically bind amyloid fibrils, see in particular p. 6, line 25. Applicants assert that the antibody of Konig et al., is raised against beta-A4 peptide, not an amyloid fibril. However, Konig establishes as well recognized in the art that amyloid fibrils are composed of beta-amyloid peptide fragments, see in particular pp. 1-5 background of Konig. In addition, Nettleship et al., of record notes that beta amyloid is commonly referred to in the art as the beta-A4 species, abbreviated as β -amyloid, beta-A4, β A-4, A-beta, A β and amyloid-beta, see in particular column 2, lines 32-37. Thus, in contrast to Applicant's assertions, Konig does teach as further evidenced by Nettleship that the immunoglobulin polypeptide is a monoclonal antibody raised against an amyloid fibril. The proteins are known to be the same. Rejection on these grounds is maintained.

Applicants arguments presented in the response of 3-16-05 are essentially the same as previously of record. In particular Applicants argue that Konig does not teach removal or opsonization in vivo. Applicants further argue that O'Nuallain notes that certain antibodies may be specific to fibrils but not native protein as support that the Konig disclosure does not support the inherent properties to removal, opsonization or binding and argue that the Konig reference is non-enabling therefore and that Becker cannot further evidence fibrillar structure.

Applicants arguments filed 3-16-05 have again been fully considered but are not persuasive. Konig already notes that the antibodies are sufficient for removal, although they do not use the *ipsis verbis* statement of "opsonization" this is the mechanistic property as provided for example by Benjamini et al., as below. Furthermore the statements with respect to O'Nuallian do not teach away whereby the Konig antibodies are already recognized as binding to in vivo plaque fibrils, see in particular immunohistochemistry. Becker is not used incorrectly whereby it evidences the fact that native protein forms fibrils. Applicants have not distinguished over the prior art or provided evidence that the antibodies of Konig are insufficient to provide all claimed effects whereby the administration is to the same patient population and where no distinguishing quantities or other limitations teach over the prior art. Rejection is maintained.

Applicants argue in the 12-20-05 response that the Konig reference is not anticipating with respect to the amount of antibody that is to be administered and that the prevention of aggregation of amyloid of Konig is a different process than the instantly

claimed removal. Applicants further cite at p. 7, first full paragraph noted case law with respect to decisions noting that anticipation may require either literal or inherent teaching of each and every limitation including dosage.

Applicant's arguments filed 12-20-05 have been fully considered but they are not persuasive. As extensively noted above in the prosecution history, the perceived difference of "preventing aggregation of amyloid" vs. "removal of amyloid" by Applicants is not distinguished, but instead is a mere reference to a description of a "different process". This "different process" is not born from evidence that distinguishes the two, but instead is a reference to a perceived "mechanism" which is not distinguished. In both cases the only measurement is of the absence or reduced accumulation of amyloid deposits. Whether the reduction or absence is one of "prevented aggregation" or "removal" has not been distinguished by either reference. Accordingly, the reference is determined to be anticipatory in that it does literally or inherently teach every limitation. The different limitations are to one of perceived mechanism, and are equivalent or the same as they are not distinguished.

It is not agreed that Konig is absent direction to any quantity or amount. The reference is clearly on point to the requirement for the antibody molecule to bind the beta amyloid antigen. The Konig reference notes quantities evaluated for binding as in immunochemistry reactions, competitive binding studies, for screening of sera and for immunoprecipitation. It is clear that the quantities here are within the skill of the artisan to be determined and may be routinely detected via analysis of antigen/antibody binding either in vitro or in vivo. Accordingly the amounts of Konig that are to be used are

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clearly determinable and would mechanistically include where any single antibody molecule interacted with its antigen so as to prevent aggregation. This amount is not distinguished from any required quantity of the instant invention directed to "amyloid removal." In both instances the quantity is apparently the same, being a sufficiency for any antibody molecule to bind its antigen. This is the mechanistic requirement of both recitations directed to "prevention of aggregation" or "amyloid removal." Moreover, the instant claims are not limited to any specific quantity and the specification is on point to the only requirement being that antigen/antibody binding occur. Accordingly, Konig is on point to the same dosage requirement as the instant invention and further instant claims and the case law noted is supportive to the teachings which are literally and inherently provided. Rejection is maintained for these same reasons of record.

14. Claims 24, 30-35 and 37-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Nettleship et al., EP613007, 8-31-1994.

Nettleship et al., teach antibodies useful in the diagnosis and treatment of mammals suffering from Alzheimer's Disease, see in particular column 7, line 39-column 8, line 18. The antibodies are specific to beta-amyloid peptides, particularly in beta-sheet conformation, but also include antibodies to alternative fragments, see in particular column 1, line 52-column 2, line 56. It is understood that the functional embodiment which characterizes the diagnostic and therapeutic relationship as disclosed in Nettleship hinges on the binding of the antibodies to the beta-amyloid peptides, see in particular reference in paragraph spanning columns 7-8 and reference to numerous assay systems suitable to detect agents which bind, column 8, lines 6-15.

In addition, the compositions are pharmaceutical compositions which include formulations for parenteral administration (other than by intestinal, i.e., subcutaneous, intravenous, etc., as understood by the skilled artisan), see in particular column 8, lines 19-42. Nettleship et al., teach the use of alternatively produced beta amyloid antibodies including to peptides which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus the reference teaches the variable or cross-reactive antibodies of the claims. It is noted that the polyclonal sera would inherently include multiple antibodies and Ig isotypes. It is further noted that the patient population includes mammals and thus encompasses humans and human antibodies, particularly of Alzheimer's patients, see in particular columns 6-7. Further the reference is effective in the treatment of Alzheimer's. Thus, the reference is deemed to be enabling for the determination of appropriate doses and routes of administration suitable for treatment. The mechanism whereby the treatment occurs, via removal of amyloid, is inherently provided.

Similar to Konig, it is true that Nettleship does not teach the definitive mechanism for the treatment provided to Alzheimer's patients via administration of antibodies to beta-amyloid. However, the mechanism of the treatment is not required for Nettleship to be enabling. It is well accepted in patent law that a newly discovered property does not make a compound or method newly patentable. Similarly here, the claiming of an old method via the use of mechanistic limitations such as by the recitation of "an amount

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effective to remove amyloid deposits" does not evidence patentability over the prior art teachings. The question is whether or not the methods are the same or different. In this analysis both methods provide the same antibodies to the same patients for the same purpose. Moreover, Nettleship notes that their method is effective for treatment of Alzheimer's and thus the mechanism is inherently provided absent convincing factual evidence to the contrary. It is Applicant's burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicant's claims. Reasons showing inherency have clearly been shown and there are no limitations to the antibodies, their amounts or routes of administration that would teach over the prior art reference. Thus, the reference teachings anticipate the claimed invention.

Applicants argue in the response of 3-30-04 that Becker also does not teach specific guidance or examples for administering such antibodies to remove amyloid deposits from patients and thus is not enabling. Applicants again refer to the Biere declaration as supportive of non-enablement and to the limitations within claim 49 which are not assertedly met.

Applicants arguments filed 3-30-04 have been fully considered but are not persuasive for the same reasons of record. The question of anticipation here is whether or not the methods are the same or different. In this analysis both methods provide the same antibodies to the same patients for the same purpose. Nettleship teaches administration of beta-amyloid antibodies effective for treatment of Alzheimer's. While Nettleship does not teach *ipsis verbis* "a method of removing amyloid deposits", these

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claim limitations are deemed to be inherently provided as the administration is the same, i.e., an amount of immunoglobulin polypeptide in an amount effective to remove amyloid deposits wherein the immunoglobulin polypeptide or fragment thereof binds to an amyloid fibril or component or precursor thereof. A prior art reference is not required to teach the mechanism of action in order meet the requirements of either anticipation or enablement. The preamble statement "removing amyloid deposits" is akin to the recitation of a mechanism. In particular, it is Applicant's burden to show unobvious difference as the PTO has insufficient resources to compare the teachings of the prior art reference and that of Applicant's claims. Reasons showing inherency have clearly been shown and there are no limitations to the immunoglobulin polypeptides (antibodies), their amounts or administration that teach over the prior art reference. There is no precedent in the cited case law to conclude that Nettleship is non-enabled. The above appears more to a question of fact to which Applicants have shown no evidence or scientific reasoning that would disprove the Nettleship teachings. Applicants question of Nettleship's enablement alludes to a question of enablement regarding the instant claims as the Nettleship teachings are not differentiated therefrom. The Biere declaration as set forth below is not effective to obviate the rejection in that it does not substantiate a conclusion that the prior art of record is non-enabled. With respect to the noted limitations at claim 49, Applicants are directed to column 1, in which Nettleship teaches that amyloid plaques or neurofibrillary tangles are mainly comprised of beta-amyloid proteins. In addition, Nettleship notes that preferred antibodies are to beta-amyloid in the β -sheet conformation. This conformation is

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believed to be the insoluble fibrillary form within neurofibrillary plaques. Nettleship et al., teach monoclonal antibodies which bind beta-amyloid in β -sheet conformation, see in particular columns 5-6, including for treatment of Alzheimer's disease, column 7. Konig et al., of record above further evidences, as recognized in the art, that amyloid fibrils are composed of beta-amyloid peptide fragments, commonly referred to in the art as the beta-A4 species, see in particular pp. 1-5 background of Konig and also Nettleship column 2, lines 32-37. It is well established that amyloid plaques or fibrils are comprised of beta-amyloid peptides commonly referred to or abbreviated as β -amyloid, beta-A4, β A-4, A-beta, A β and amyloid-beta. Thus, in contrast to Applicant's assertions, Nettleship does teach that the immunoglobulin polypeptide is a monoclonal antibody raised against an amyloid fibril corresponding to "fibrillar amyloid" as noted in Konig and to beta-amyloid in beta-sheet conformation as noted in Nettleship. The proteins are known to be the same. Rejection on these grounds is maintained.

Applicants arguments presented 3-16-05 are essentially as of record. In particular Applicants argue that Becker does not sufficiently teach removal or opsonization and that the Biere decaration teaches away from such properties.

Applicants arguments filed 3-16-05 have been fully considered but are not persuasive for the same reasons of record. The antibodies are those to firbrillar formations, bind and prevent aggregation, stimulate removal and opsonization as they are noted to be effective for treatment of Alzheimer's disease. Accordingly, rejection is maintained.

Applicants similarly argue in the 12-20-05 response that the Nettleship reference is also not anticipating with respect to the amount of antibody that is to be administered as Nettleship is merely directed to antibodies for treatment of mammals suffering from Alzheimers disease.

Applicant's arguments filed 12-20-05 have been fully considered but they are not persuasive. As extensively noted above in the prosecution history, the perceived difference of Nettleship vs. Applicant's recitation of "removal of amyloid" is a perceived difference in mechanism which is not distinguished. As in Konig Nettleship is not silent to any quantity. In contrast, Nettleship is on point to the sufficiency or requirement that the antibody bind antigen. A single molecular interaction of antigen/antibody then is sufficient to effect treatment. In both cases the only measurement that is provided is one of reduced symptomatology as in the absence or reduced accumulation of amyloid deposits. Whether the reduction or absence is one of "treatment" or "removal" has not been distinguished by either reference. Accordingly, the reference is determined to be anticipatory in that it does literally or inherently teach every limitation. The different limitations are to one of perceived mechanism, and are equivalent or the same as they are not distinguished.

As set forth above in the grounds of rejection, Nettleship is on point to the requirement for the antibody molecule to bind the beta amyloid antigen. The reference notes quantities that "inhibit neurotoxic effects", see column 1, lines 52-56, including several noted assays for evaluation and specificity to the beta-sheet conformation or as evaluated for binding as in immunochemistry reactions and competitive binding studies.

Again, it is clear that these quantities are well within the skill of the artisan to be determined as routinely detected via analysis of antigen/antibody binding either in vitro or in vivo. Accordingly the amounts of Nettleship are clearly determinable and would mechanistically include where any single antibody molecule interacted with its antigen so as to bind, prevent neurotoxic effect and to provide treatment. This amount is not distinguished from any required quantity of the instant invention as directed to "amyloid removal." In both instances the quantity is apparently the same, being a sufficiency for any antibody molecule to bind its antigen. This is the mechanistic requirement of both the instant specification, claims and the Nettleship reference. Accordingly, Nettleship is on point to the same dosage requirement as the instant invention and the teachings are literally and inherently provided. Rejection is maintained for these same reasons of record.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 24, 30-35 and 37-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konig et al., WO96/25435, 22 August 1996, Nettleship et al., EP613007, 8-31-1994, Schenk cumulative US Patents 6,743,427 and 6,787,523 and Immunology: a short course, Benjamini & Leskowitz Ed., Wiley-Liss, Inc., New York, NY, page 142.

Schenk US Patent No., 6,743,427, June 1, 2004 and Schenk US Patent No., 6,787,523, September 7, 2004 are cumulative, see in particular the '427 patent is a continuation in part of the '523 patent. Thus, the rejections are noted together. The claims of the 6,743,427 are most relevant in that the claims are directed to a method of prophylactically or therapeutically treating Alzheimer's disease comprising administering to the patient an effective dosage of a pharmaceutical compositions comprising an antibody that specifically binds to an epitope within residues 1-12 of Abeta wherein the isotype of the antibody is human IgG1, see in particular claims 1-19. However, the details of the rejection will be set forth with citation to the '523 patent, reflecting the disclosure most similar to the effective filing date of 12-2-1997.

The '427 and '523 patents each teach treatment of Alzheimer's disease via either administration of peptide to promote the production of beta amyloid antibodies (Active immunization) within the host or via direct administration of antibodies (Passive immunization) reactive to beta amyloid, see in particular columns 1-4, 10-11, column 14,

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lines 55-63, and columns 33-34 Passive immunization. The Patent teaches that the mechanism whereby the active immunization treatment is effective is via the stimulation in vivo of an antibody response with high titer sufficient whereby the antibodies bind to and remove the amyloid plaques from brain, see in particular columns 13-33. Hence the mechanism disclosed in the patent is the same as that claimed, ie., "whereby the antibody or immunoglobulin polypeptide or fragment thereof (is) in an amount effective to remove amyloid deposits, wherein the antibody or immunoglobulin polypeptide or fragment thereof (binds to and) opsonizes an amyloid fibril and induces removal of amyloid deposits". As in claims 30-32 and 47-49, the antibodies may be monoclonal, see in particular column 10, line 64, human, column 11, lines 15-17, humanized, column 11, lines 9-14 in particular but also column 11, lines 1-55. In particular, such humanized antibodies or portions where immunoglobulin specific chains or genes are alternatively linked constitute antibodies that are "chimeric" or "having cross-isotype reactivity" thereby anticipating claims 33-34 and 39. The antibodies may be labeled as in for detection in vitro or in vivo, see in particular Figures 5-14. The antibodies may constitute fragment portions such as Fv, Fab etc, see in particular column 11, lines 40-44, and single chain, column 11, line 43, corresponding to claims 37-38. As previously detailed the antibodies are specific to beta amyloid protein of Alzheimer's disease, corresponding to non-light chain amyloid, see also column 9. The treatment is noted to be inclusive of humans and human patients, see in particular column 8. Claim 43 presents the limitation, "wherein the antibody or immunoglobulin polypeptide or fragment thereof is reactive with an amyloid fibril other than the amyloid fibril or

component or precursor thereof against which the immunoglobulin polypeptide or fragment thereof was raised.” This is deemed to be an intrinsic property of the noted antibodies which are made either in vitro or in vivo and then isolated and or proliferate in vivo such that the progeny or administered antibodies react with amyloid fibrils in vitro or in vivo but those fibrils are other than the ones against which the antibodies were raised, a process mediated via B-cell production. As in columns 8 and 13-17 the treatment is via administration of multiple molecules (concentration dependent) and with carrier (claims 44-45).

Konig et al., teach as set forth above. In particular Konig teaches methods of diagnosis, screening and therapeutics for treating unique forms of amyloid peptide deposition using antibodies. Konig et al., teach administration of monoclonal antibodies that bind amyloid fibrils, see in particular claims 9-20 and pp. 6-8 for treatment of Alzheimer’s disease. The antibodies specifically bind amyloid fibrils, see in particular p. 6, line 25. Thus, the reference teaches a method which comprises treating a patient having an amyloid deposition disease by administration of an immunoglobulin polypeptide which binds to an amyloid fibril. Konig further teaches that the antibody treatment is effective in a method for the prevention of aggregation of beta amyloid peptide by administration of the antibody, see in particular p. 7, lines 21-23, p. 13, lines 17-20, p.14, lines 6-11 and p. 25, lines 14-18. The antibodies can be provided in sterile saline or a pharmaceutically acceptable carrier such as Keyhole Limpet Hemocyanin, see in particular p. 17. The antibody intrinsically opsonizes upon binding, as evidenced by Benjamini et al., which teach at p. 142 that IgG immunoglobulin antibodies bind and

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mediate opsonization or removal via phagocytosis. Thus, the artisan would equate the mechanistic recitation of inhibiting formation, removal or modulation of amyloid deposition as being achieved. The antibodies may be labeled by biotinylation or with radioactive tags such as ³⁵S-Met, see in particular p.22. Konig further notes at p. 5-7 suitable cross-reactive antibodies and epitopes for various modifications. Specific embodiments of monoclonals are disclosed from p. 19-23.

Nettleship et al., teach as set forth above. In particular Nettleship teaches antibodies useful in the diagnosis and treatment of mammals suffering from Alzheimer's disease, see in particular column 7, line 39- column 8, line 18. The antibodies are beta-amyloid peptides, particularly in beta-sheet conformation, but also include antibodies to alternative fragments, see in particular column 1, line 52-column 2, line 56. It is understood that the functional embodiment which characterizes the diagnostic and therapeutic relationship as disclosed in Nettleship hinges on the binding of the antibodies to the beta-amyloid peptides, see in particular reference in paragraph spanning columns 7-8 and reference to numerous assay systems suitable to detect agents which bind, column 8, lines 6-15. In addition, the compositions are pharmaceutical compositions which include formulations for parenteral administration (other than by intestinal, i.e., subcutaneous, intravenous, etc., as understood by the skilled artisan), see in particular column 8, lines 19-42. Thus, the reference appears to be enabling for the determination of appropriate doses and routes of administration suitable for such binding, inhibition of formation, removal or modulation of amyloid deposition to occur. Nettleship et al., teach the use of alternatively produced A

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antibodies including to peptides which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus the reference teaches the variable or cross-reactive antibodies of the claims. It is noted that the polyclonal sera would inherently include multiple antibodies and Ig isotypes. It is further noted that the patient population includes mammals and thus encompass humans and human antibodies, see in particular columns 6-7.

Applicants specification at pp. 14-16 also teach the routine of one of skill in the art to produce humanized and chimeric antibodies.

Neither Konig nor Nettleship specifically teach the mechanistic effects of antibody administration as specifically recited in the claims, i.e., the removal or opsonization of amyloid deposits or the modulation of formation of amyloid deposits. However, Schenk teaches the mechanistic basis of antigen and antibody treatment in removal of amyloid plaques via antibody binding and opsonization via phagocytosis and demonstrates it in vivo in brain tissues. Konig et al., teaches that antibody administration is effective to prevent aggregation or for extraction of amyloid deposits and Nettleship teaches the use of antibody administration for the treatment and prevention of Alzheimer's disease mediated via preventing and treating amyloid deposition. However, Benjamini et al., teach as recognized in the art that antibody binding mediates opsonization and removal of IgG bound material in the host.

Thus, it would have been *prima facie* obvious to the skilled artisan to utilize either the antibodies of either Schenk, Konig or Nettleship for the *in vivo* administration and treatment of patients, particularly with Alzheimer's disease. Further it would have been *prima facie* obvious based on the teachings of Schenk, Konig, Nettleship and Benjamini that such treatment is effective to remove beta-amyloid thus treating Alzheimer's via modulating the levels of amyloid in patients. One of skill in the art would have been motivated to provide such a method based on the cumulative reference teachings and the recognition in the art of opsonization based upon antibody binding to beta-amyloid. The effective amounts are provided by the antibody compositions effective for binding and routing. Further, one skilled in the art would have expected success using such a method based upon the high skill in the art of antibody technology and the combined teachings of Schenk, Konig, Nettleship and Benjamini in the treatment of amyloid deposition disease with non-light chain, beta-amyloid antibody, particularly in Alzheimer's disease. Thus, for the aforementioned reasons, the claimed invention is rendered obvious to the skilled artisan.

Applicant's argue in the response of 6-27-03 that the Konig reference does not disclose a method of administering antibodies to a patient to remove amyloid deposits from the patient and that according to the declaration of Dr. Biere antibodies used as diagnostics are not suggestive of effectiveness in removing amyloid from a patient. Applicant's argue that the 369.2B antibody was not tested for *in vivo* administration and that it's use would not be predicted to remove amyloid in an *in vivo* system. Applicants argue that Becker (Nettleship) does not teach a method of treatment comprising

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administering antibodies to patients to remove amyloid deposits and the discussion is hypothetically of therapeutic purposes. Applicant's argue that it was not predictable that the antibody would be effective in removing amyloid deposits.

Applicant's arguments filed 6-27-03 have been fully considered but are not persuasive. In particular, the Examiner notes that the Konig and Becker (Nettleship) references each teach the administration of beta amyloid antibodies for therapeutic use in Alzheimers treatment. Further, the Benjamini supports the artisan's knowledge of opsonization and removal of material via antibody IgG binding within the host. The references each evidence binding specificity. It is further noted that the mechanism by which the methods effect their treatment is unimportant. The similarity or difference as to the method steps is. In instant case, the steps of the methods within the prior art and instant claims appear identical in that the same antibodies are provided to the same patient population for the same purpose/utility, i.e., the treatment of Alzheimer's as explicitly stated in both prior art references. Moreover, there are no limitations within instant claims as to the route, quantity, type of antibody or otherwise that would indicate any difference in the ability of particular antibodies to be successful or not in the claimed method. In short, both the prior art and instant claims evidence the applicability of any antibody in the method to the extent that the antibodies bind to an amyloid fibril or component or precursor thereof. Thus, the cumulative reference teachings render the invention obvious to the artisan.

Applicants arguments in the response of 3-30-04 are as essentially of record. In particular it is Applicants position that the Konig and Nettleship references fail to teach

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removal and that the Benjamini et al., reference does not cure this deficiency.

Applicants refer to Dr. Biere's declaration in support of an unexpected discovery.

Applicants arguments filed 3-30-04 have been fully considered but are not persuasive. Even should the Konig and Nettleship references be found to be non-anticipatory, because it fails to *ipsis verbis* teach removal of amyloid via antibody binding, the Benjamini reference teaches the art recognized mechanistic property of antibody/antigen interactions *in vivo*, specifically binding, opsonization and removal of immunoglobulin (Ig) bound material. In contrast, the Benjamini reference directly supplements the cited deficiency. Hence, as previously set forth, the cumulative reference teachings render the claimed invention obvious to the artisan.

Applicants argue in the 3-16-05 response, as essentially of record. In particular Applicants argue that the references do not meet the limitations of removal and opsonization. In contrast, the references are on point to removal and effective to treatment. Benjamini notes the properties that binding provides to opsonization of antigen. The specificity of the antibodies of the references are the same, i.e., that of fibrillar amyloid and no evidence teaches that such properties are not provided by this specificity. Thus, rejection is maintained. As to the newly issued patent of Schenk, this reference further evidences that the specificity would appear to be all that is required, further supporting the anticipation and enablement of the prior art references and evidencing the mechanistic properties of the noted antibodies in removal and opsonization.

Applicants argue in the 12-20-05 and 3-6-06 responses that the 1.131

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declaration and exhibits obviate rejection and that the additional references do not meet an effective dosage or amount of the antibody so as to remove amyloid deposits.

Applicant's arguments filed 12-20-05 and 3-6-06 have been fully considered but they are not persuasive as noted above. The declaration and evidence referred to therein is not in scope with the claimed invention. Further, the amounts as directed in the Konig, and Nettleship references are not deficient where the amount is on point to the mechanistic requirement that the antibody molecule react with its antigen. Accordingly the amounts are effective to remove amyloid absent factual evidence to the contrary. The limitations as to mechanism and amount are literally and/or intrinsically provided. Benjamini is further supportive of equivalent mechanistic recitations.

Declaration of Dr. Biere

17. The declaration under 37 CFR 1.132 by Dr. Biere has been fully considered but is not persuasive. Dr. Biere notes that the focus of amyloidosis research at the time of the invention relates to inhibiting production or enhancing clearance of the precursor protein and not to therapy via the use of antibodies in removal. Dr. Biere further suggests that the successful use of antibodies to clear amyloid was unexpected. Dr. Biere further notes that the binding of antibodies is not predictive of effector function.

The declaration has been fully considered but is not persuasive. The relevant issue is whether or not there is an obvious difference between the prior art teachings and Applicant's claims. The prior art teachings are directed to the invention of administration of beta amyloid antibodies for the treatment of Alzheimer's disease. Both prior art references and applicant's claims indicate that any antibody that binds amyloid

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is effective and useful in the treatment. There is no evidence or limitations in the claims or specification that indicate that anything other than binding is required such that removal and/or opsonization occurs. In fact, Applicants claims are structured such that any antibody that binds is capable of removal. Moreover as Benjamini teaches that immunoglobulin (Ig) mediated binding, removal and opsonization are recognized as one in the same, no differences can be discerned. Thus, Benjamini evidences in contrast to Biere, that the mechanism of removal by immunoglobulin binding is expected. The declaration provides no evidence as to a direct comparison or to unobvious difference in the claimed methods in comparison to the prior art. Moreover, both of the prior art references are not limited to binding studies. In fact, both the prior art references teach the effectiveness of the antibodies as therapeutics in Alzheimer's. In contrast to Dr. Biere's position the teachings are anticipated and expected. The declaration fails to evidence that the prior art references are non-enabling. Thus, the declaration is ineffective to overcome the prior art teachings and recitations of mechanism fail to distinguish over the prior art.

Status of Claims

18. No claims are allowed.

Conclusion

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Thursday from 7:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at (571) 272-0867.

Sharon L. Turner, Ph.D.
April 25, 2006



SHARON TURNER, PH.D.
PRIMARY EXAMINER

4-25-06